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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/424,519	03/03/2000	JAMES B. MITCHELL	175931	8084

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EXAMINER
KWON, BRIAN YONG S

ART UNIT	PAPER NUMBER
1614	19

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/424,519	MITCHELL ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-21,23 and 28-49* is/are pending in the application.

4a) Of the above claim(s) *4-21, 31-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,28-30 and 49* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 March 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Summary of Action

I. The rejection of claims 2-3, 22, 24 and 26 under 35 USC 112, first paragraph, will not be maintained in light of the amendment.

II. The rejection of claims 1-3 and 22-27 under 35 USC 102(e) as being anticipated by Bernstein will not be maintained in light of the Declaration.

III. The rejection of claims 1-2 under 35 USC 102(e) as being anticipated by Wang et al. will not be maintained in light of the Declaration.

IV. Claims 1, 28-30 and 49 are rejected under 35 USC 112, first paragraph.

V. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action.

V. There are no arguments in applicants Response.

Status of Application

1. By Amendment filed February 15, 2002, claims 2, 3, 22 and 24-27 have been cancelled; claims 1, 4, 6, 8, 12, 14, 21 and 23 have been amended; and claims 28-49 have been newly added.

As indicated in Paper No. 6, Claims 4-21 were withdrawn from consideration by the Office as being directed to a non-elected species. Newly added claims 31-48 are directed to an invention that is independent or distinct from the invention originally elected species, Tempol. It is noted that applicant originally has received an action on the merits for the originally elected species, this invention has been constructively elected by original presentation for prosecution on

the merits. Accordingly, claims 31-48 are withdrawn from consideration as being directed a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1, 23, 28-30 and 49 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 1 is rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly amended claim relates to a method for the therapeutic treatment of cancer in an animal at risk for developing a cancer or having a cancer due to an inherited genetic defect in the abl, bcl2 or p53 gene, comprising administering nitroxide or prodrug thereof represented by Formula I or II, namely Tempol.

Although the instant specification discloses the efficacy of a nitroxide, namely Tempol, in delaying the onset or progression of tumors related to p53 tumor suppressor gene mutation (Examples 1-2), nowhere in the specification clearly point out the conclusion of the efficacy of Tempol in treating all cancers or cancers due to the genetic defect in the abl or bcl2 or cancers that may not related to p53 gene mutation.

Although the instant specification recites ataxia telangiectasia, Cowden's disease, Torre's syndrome, Gardner's syndrome, Wiskott-Aldrich syndrome, Peutz-Jeghers syndrome, Bloom's syndrome, Faconi's syndrome, Wemers syndrome, Chediak-Higashi syndrome, retinoblastoma, Beckwith-Wiedeman syndrome and neuroblastoma as examples of inherited genetic defects that predispose humans to developing cancer (page 6, lines 16-21 of the specification), the specification fails to provide sufficient guidance that all above-mentioned cancers can be treated with a vast number of compounds represented by formula (I) or (II) or prodrugs, more specifically Tempol. The specification provides insufficient guidance to ascertain that p53 "knock-out" mice model study could be a representative model for other types of cancer regulatory gene or tumor suppressor gene such as abl or bcl2. Furthermore, the specification fails to provide insufficient written description to support the use of the claimed composition in the therapeutic treatment of cancers due to the abl or bcl2 genetic defects.

With the exception of cancers related to p53 gene mutation, the skill artisan cannot envision the method of treating cancers that are related to the genetic defect in abl or bcl2 gene. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of the treatment. Applicants claim for the therapeutic treatment of those cancers due to abl or bcl2 of does not meet the written description provision of 35 USC 112, first paragraph.

See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

3. Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The reasoning of this rejection is analogous to the rejection of claims 1-3 under 35 USC 112, first paragraph, rejection (pages 2-4 of O.A. mailed on 9/18/02, Paper No. 16).

4. Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The reasoning of this rejection is analogous to the rejection of claims 22, 24 and 26 under 35 USC 112, first paragraph, rejection (page 5-7 of O.A. mailed on 9/18/02, Paper No. 16).

5. Claims 28-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention .

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The claimed invention relates to a method for the prophylactic or therapeutic treatment of cancer in an animal at risk for developing a cancer or having a cancer due to an inherited genetic defect selected from the group consisting of ataxia telangiectasia, Cowden's disease, Torre's syndrome, Gardner's syndrome, Wiskott-Aldrich syndrome, Peutz-Jeghers syndrome,

Bloom's syndrome, Faconi's syndrome, Wemers syndrome, Chediak-Higashi syndrome, retinoblastoma, Beckwith-Wiedeman syndrome, and neuroblastoma, comprising administering nitroxide or prodrug thereof represented by Formula I or II, namely Tempol.

(2) The state of the prior art

The art teaches the use of Tempol in protecting radiation-induced alopecia and protecting photoaging, sunburn and skin cancer resulted from sunlight exposure in vivo. Furthermore, the art teaches the use of Tempol in inhibiting the growth of several mammalian cancer cell lines such as adenocarcinoma MCF-7 cells, HL-60 cells and OVCAR-3 carcinoma cells in vitro. However, the art does not teach the use of the claimed nitroxide, namely Tempol, for the prophylactic or therapeutic treatment of any cancers or a cancer due to an inherited genetic defects selected from the group consisting of ataxia telangiectasia, Cowden's disease, Torre's syndrome, Gardner's syndrome, Wiskott-Aldrich syndrome, Peutz-Jeghers syndrome, Bloom's syndrome, Faconi's syndrome, Wemers syndrome, Chediak-Higashi syndrome, retinoblastoma, Beckwith-Wiedeman syndrome, and neuroblastoma.

(3) The relative skill of those in the art

The relative skill of those in the art is high. Applicant's specification does not enable the public to determine which types of above-mentioned cancers can be prevented or treated by administration of the nitroxide, Tempol without undue amount of experimentation.

(4) The predictability or unpredictability of the art

The unpredictability of the cancer therapy is very high. Treatment or prevention of different types of cancers requires undue amount of experimentation. Furthermore, the skill artisan cannot predict from the instant specification disclosure of using Tempol in delaying the onset of tumor in p53 tumor suppressor gene deficient mice study that Tempol would be effective in preventing or treating any cancers or cancers mentioned above that are may not related to p53 gene.

(5) The breadth of the claims

The claims are very broad. The scope of the instant claim encompasses not only the prophylactic or therapeutic treatment of ataxia telangiectasia, Cowden's disease, Torre's syndrome, Gardner's syndrome, Wiskott-Aldrich syndrome, Peutz-Jeghers syndrome, Bloom's syndrome, Faconi's syndrome, Wemers syndrome, Chediak-Higashi syndrome, retinoblastoma, Beckwith-Wiedeman syndrome or neuroblastoma that is related to any types of inherited genetic defects, but also the prophylactic or therapeutic treatment of any cancer(s), comprising administering a vast number of compounds represented by formula (I) or (II).

(6) The amount of direction or guidance presented

The specification and the Declaration, filed 1/16/03, all disclose the results of study involving Tempol or sugar-water treated p53 knock-out mice (KO1). The study shows that both Templ-treated mice and sugar-water-treated mice group ultimately develop cancers, but the percent survival is increased in Tempol-treated group (page 16, lines 4-6). Although the specification and the Declaration provide enabling disclosure for delaying onset or progression

of cancers due to p53 gene mutations with the administration of Tempol, none of the specification or the Declaration provides enabling disclosure for the claimed prophylactic or therapeutic treatment of any cancers or above-mentioned cancers that may not related to p53 gene mutations.

In addition, the instant specification (page 16, lines 4-6) and the Declaration provide no evidences that said cancers can be completely controlled or prevented.

(7) The presence or absence of working examples

As stated above, the specification and the Declaration, filed 01/16/03, fail to provide adequate representation to ascertain that p53 "knock-out" mice model could be a representative model for the entire genus of cancer regulatory gene or tumor suppressor gene. Both specification and the Declaration fail to provide adequate representation regarding the conclusion of the efficacy of Tempol in treating abl or bcl2 gene related cancers from applicant's showing of the efficacy of Tempol in increasing the percent survival in p53 "knock-out" mice model study. Furthermore, both specification and the Declaration fail to provide adequate representation for the public to determine which types of cancers mentioned abvoe would fall within the p53 gene mutation and be susceptible to the treatment of Tempol.

(8) The quantity of experimentation necessary

Since the efficacy of Tempol in preventing or treating various types of cancers mentioned above or cancers that may not related to p53 gene mutation cannot be predicted from a priori but

must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine the all of would not affect the property of the peptide.

Conclusion

6. Claim 23 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

8. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600